WEIL'S DISEASE IN GLASGOW SEWER WORKERS

BY

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The most striking feature about the literature of Weil's disease is the lack of reference to infection in sewer workers. Environmental factors appear highly favourable, yet with the exception of isolated cases such as recorded by Capellini and Berzi (1932) and Knack (1933) no evidence of such infection was produced till Fairley (1934) described a typical case of Weil's disease in a London sewer worker, proved by serological tests and by isolation of the organism from inoculated guinea-pigs to be caused by *Leptospira icterohaemorrhagiae*. Seven other cases recorded by the same author gave histories of severe illnesses associated with jaundice, and their sera still showed the presence of antibodies to *L. icterohaemorrhagiae*. One further case with a typical history and post-mortem findings was discussed. The author pointed out that he was dealing with a limited number of workers (forty-five), and though only those with suggestive histories were investigated the evidence indicated that leptospiral infection was a very grave occupational risk in sewer-men. Alston (1935) described three further cases occurring in the interval since Fairley's paper, and mentioned another two. In a review of the epidemiology of Weil's disease Alston and Brown (1937) pointed out that nineteen cases with five deaths had occurred in London sewer workers between July, 1933, and February, 1937. No cases among similar workers in other parts of the country were reported, although the above figures suggested that leptospiral infection was likely to prove a grave occupational risk. The occurrence of Weil's disease in Glasgow sewer workers was first appreciated with the admission to the Royal Infirmary of the following case.

Case History

A man aged 34 was taken ill on September 22, 1937, with severe pains in the leg muscles and a slight temperature. Symptoms rapidly became more severe and were accompanied by a painful backache. Fever and constitutional upset were present, and at first a diagnosis of influenza was made. Anorexia was noted, with nausea and vomiting. Jaundice was first seen on September 28. Epistaxis occurred on the 27th and more severely on October 1. When admitted to hospital on October 2 the patient was collapsed (temperature 97° F.), and he died in a few hours.

POST-MORTEM REPORT

The body is that of a well-nourished young man. Severe jaundice is present. The skin shows multiple petechiae with a herpes-like eruption round the mouth.

Pericardium.—A few petechiae appear on both visceral and parietal surfaces.

Heart.—(360 grammes.) There is evidence of an old rheumatic endocarditis on both the mitral and the aortic valves, with adhesion of the edges of the aortic cusps. Recent vegetations are scattered over both valves. The heart is otherwise normal.

Pleurae.—Many adhesions occur round the base of the right lung.

Lungs.—(Right, 1,050 grammes; left, 1,000 grammes.) Both organs show very marked oedema, with an early hypostatic pneumonia.

Trachea and Oesophagus.—Normal.

Peritoneum.—Normal.

Stomach and Intestines.—The stomach shows multiple haemorrhagic erosions, and contains blood-stained material. The intestine is dilated, and contains very dark changed blood.

Liver.—(2,000 grammes.) The organ is large. The capsule is not wrinkled. On section a background of liver tissue shows considerable fatty change, but on top of this there appears to be a diffuse necrosis with pronounced bile staining. No bile is present in the gall-bladder or the bile passages.

Spleen.—(105 grammes.) Small and normal in appearance.

Kidneys.—(Right, 200 grammes; left, 250 grammes.) Both organs are large and soft, and on section give the appearance of fatty degeneration with pronounced bile staining.

Brain.—(1,600 grammes.) The organ is very oedematous and soft, and on section reveals multiple scattered petechiae. The cerebrospinal fluid shows bile staining.

BACTERIOLOGY

Blood specimen was taken on October 2: Schüffner's sero-reaction was positive to *L. icterohaemorrhagiae* 1 in 1,000 and negative to *L. canicola*. Levaditi-stained preparations of the liver obtained at necropsy on October 4 showed much granular debris suggestive of phagocytosed and broken-down spirochaetes. One or two identifiable leptospirae were, however, discovered after prolonged search. The organism was not isolated, probably because the blood was taken on Saturday evening and was not received till Monday. Blood clot and liver were inoculated into guinea-pigs on that day, but no evidence of leptospiral infection was found, nor did reinoculation of their tissues produce any disease. The sero-reaction of all animals remained consistently negative to *L. icterohaemorrhagiae*.

Investigation of Deaths of Sewer Workers

This evidence that Weil's disease was occurring in the Glasgow area stimulated me to investigate the incidence of infection, and through the courtesy of the public health authorities details were obtained of deaths among sewer workers for the past three years. Five men other than the case reported above had died, and of these two had suspicious histories.

A. B., aged 60, died on September 19, 1935, death being certified as due to acute yellow atrophy of the liver. This man was ill for about a week. At first the illness was indefinite and did not seem severe, but after a few days jaundice appeared, the patient rapidly became acutely ill, and he died. The physician in charge agreed that this could easily have been a case of Weil's disease.

C. D., aged 51, died on September 20, 1937, from an affection certified as acute cholecystitis. The illness in this case was very similar to the above. Jaundice developed about the fourth or fifth day. Severe haematemesis occurred before death after about ten days' illness. Here again the attendant physician agreed that a diagnosis of Weil's disease would have accounted for the symptoms.

One other sewer worker died on October 12, 1935, of a rather chronic lobar pneumonia with a terminal acute phase. At that time he gave a history of "sewer-gas poisoning" four years earlier. As will be seen later, this diagnosis almost certainly indicated Weil's disease.

Investigation of Non-fatal Cases

The evidence that three men had died from acute illnesses suggestive of, or proved to be, Weil's disease indicated that leptospirosis was likely to be as great a problem in Glasgow as it was in London. Again through the good offices of the public health authorities it was arranged that all the Glasgow sewer workers should be tested.

Methods.—Blood was obtained by venepuncture, and the serum was tested for the presence of antibodies to

L. icterohaemorrhagiae by Schüffner's method as described by Davidson *et al.* (1934). Living cultures of leptospira (Schüffner's non-virulent Wijnberg strain) and of *L. canicola* (both obtained from Dr. J. Smith, Aberdeen) were used as antigens, and the titre of a positive serum was the highest dilution showing lysis of leptospira. The specificity of this method has been amply proved (Schüffner, 1934; Smith and Davidson, 1936; Stuart, 1938), and non-specific antibodies even at a dilution as low as 1 in 10 have never been found.

Thirty-five men were examined out of a total of thirty-six engaged in this branch of public service in Glasgow, and six were found to be positive (see Table). In five cases

Particulars of Six Cases in which Glasgow Sewer Workers gave a Positive Sero-reaction

Case No.	Age (Years)	Nature of Employment	History of Illness	Schüffner Sero-reaction to L. icterohaemorrhagiae
1	46	12 years sewer-man	"Influenza," 1935, two months' duration; marked pains in legs. Jaundice +	Positive 1 : 30
2	46	13½ years sewer-man; 1½ years waste-man	"Sewer-gas poisoning," 1932, seven weeks' duration; debility. Jaundice +	„ 1 : 300
3	57	12 years winchman; 16 years sewer-man	"Influenza," 1931, five weeks' duration; fever and pains in limbs. No jaundice	„ 1 : 10
4	57	35 years sewer-man	Severe illness, 1927, two months' duration; high fever; haematuria. Jaundice (?)	„ 1 : 300
5	43	12 years sewer-man; 4 years foreman	"Influenza," 1926, two months in bed; prolonged convalescence. Jaundice +	„ 1 : 100
6	63	30 years sewer-man	"Sewer-gas poisoning," 1910, 10 weeks' duration; headache, vomiting, and fever began. No further recollection	„ 1 : 100

the serum titre leaves no doubt about the diagnosis. Case 3 is more dubious, but the very suggestive history is, I feel, strongly in favour of a definite leptospiral infection.

Isolation of Leptospirae from Sewer Material

Buchanan (1927) first demonstrated the possibility of isolating virulent leptospirae from non-living material by inoculating roof-slime of an infected mine into guinea-pigs. Davidson *et al.* (1934), following Appleman's technique, isolated leptospirae from floor washings of fish-cleaning establishments. Alston succeeded in isolating *L. icterohaemorrhagiae* from two out of thirty specimens of slime and mud from sewers. Young guinea-pigs, 300 grammes in weight, were used, and a marked difference in the susceptibility of such animals was recorded. Inoculation was subcutaneous or by scarification. The method by which leptospirae were recovered was not recorded, but Alston concluded that subcutaneous inoculation or scarification was likely to be better than intraperitoneal injection.

In the present investigation young guinea-pigs about 6 weeks old were used, rectal temperatures were taken daily, and blood was cultured from heart puncture whenever a rise of temperature seemed significant. If the animals remained healthy they were killed, usually between the second and third weeks, and their kidneys inoculated into further animals. Sera were tested by Schüffner's method for the presence of antibodies to *L. icterohaemorrhagiae* whenever blood was withdrawn and after the animals were killed. Twenty-eight specimens of slime and silt from the floors of sewers were inoculated by various methods. Twenty were rubbed into the shaved and scarified skin of the abdomen without success; six were inoculated by immersing the animal (Appleman's technique, as practised by Davidson *et al.*) and two by intraperitoneal inoculation, but leptospirae were not recovered. Finally ten specimens were injected subcutaneously into the groin. Some degree of local sepsis was encountered in using this technique, and temperature records were valueless as a guide to leptospiral infection, but leptospirae were recovered from one animal by heart puncture on the seventh day after inoculation. The animal, when killed five days later, had typical Weil's disease. None of the other animals inoculated by this or other methods showed any evidence of leptospirosis, nor did they develop serum antibodies to *L. icterohaemorrhagiae*, which might have suggested subclinical infection. The specimen from which leptospirae were recovered was inoculated by one method only, and therefore, although I believe subcutaneous inoculation to be best, I can produce no definite evidence on the matter.

Isolation of Leptospirae from Sewer Rats

Only two rats were obtained direct from the sewers. Both had positive sero-reactions (1 in 30) to *L. icterohaemorrhagiae*, and from one of them leptospirae were recovered in pure culture. Guinea-pigs were not inoculated. It was, of course, impossible to determine the incidence of leptospiral infection from such small figures, but the suggestion that it was high was borne out by similar findings in rats from a local abattoir where communication with the sewers was easy. Here, out of thirteen adult rats examined, eleven had a positive sero-reaction to *L. icterohaemorrhagiae*, and in eight of these leptospirae were detected by kidney histology, kidney culture, or guinea-pig inoculation.

Discussion

In the past three years three men appear to have died from Weil's disease and a fourth has been ill but has recovered. In the group of present workers six out of a total of thirty-six show evidence of past infection. The incidence of infection is less than the 24.2 per cent. recorded by Smith and Davidson in fishworkers, but the death rate appears higher than the 10 per cent. suggested by Schüffner from his wide Continental experience. It has not been possible to obtain records of deaths earlier than the above period, and the apparent severity of infection in local sewer workers may be only a chance observation. In any case, my findings fully support the evidence of Fairley and of Alston *et al.* that leptospiral infection is very definitely an occupational risk in sewer workers. All factors are favourable to the development of human leptospirosis. Sewer rats are heavily infected, and the excreted leptospirae can remain alive in sewer slime. The reaction of such material is probably of paramount importance in determining leptospiral viability. According to Walch-Sorgdrager *et al.* (1938) the ideal *p*H for the maintenance of living leptospirae is 7.3 to 7.7, but they will tolerate a slight acidity of *p*H 6.76. The specimens of slime, water, and mud obtained from Glasgow sewers had reactions from *p*H 6.9 to *p*H 7.4, and Alston *et al.* state that specimens of mud from London sewers were very nearly alkaline. Workers are liable to get cuts and scratches in the course of their duties; gloves cannot be worn with convenience, and in spite of protective clothing sewer material is apt to soak clothes and to splash into mouths and eyes.

It has been suggested that infections seem to occur especially when men are working in overflow sewers. Such sewers are particularly haunted by rats, and are coated with stagnant slime except when washed out by abundant rainfall. The possible influence of rainfall on the incidence of human leptospiral infection has been investigated, but no definite evidence has been obtained. No infection is likely when men are working in fast-running sewers or where chemical effluents are present. Rats, indeed, are uncommon in such places. No distinct seasonal incidence is apparent, although the three fatal cases occurred in September; other cases have been found in January, May, July, and December.

The lack of clinical recognition of these cases is not surprising. The diagnosis of Weil's disease is chiefly dependent on the knowledge that such infection is possible and, certainly in the milder non-jaundice cases, is entirely dependent on the laboratory. With the exception of the fairly recent work in London, evidence that sewer workers are liable to infection has been singularly lacking, but with the recognition of such a possibility one can expect an increasingly accurate diagnosis of the condition and a corresponding saving of life through early serum therapy. Probably it will be found that Weil's disease is only an occupational risk of sewer workers in large cities where the men actually enter the ducts. In smaller towns, where work is mainly on the surface, the risk of infection must be infinitely less.

Laboratory diagnosis in the first week of the disease is difficult, but should always be attempted, since serum therapy is so valuable at this stage. Direct examination of blood plasma for living leptospirae will occasionally be successful, and the inoculation of suitable guinea-pigs will reveal leptospirae in the peritoneal fluid after three or four days. After the first week, examination of the serum by Schüffner's method gives a ready clue to the condition, and a rising titre will exclude a positive result from past infection. Further, a present infection usually gives much higher titres. As an indication of previous infection a positive sero-reaction is very valuable. In the present series a positive result has been obtained twenty-seven years after an infection suggestive of Weil's disease. It is possible, however, that a positive reaction may occasionally not persist in milder cases. No evidence has yet been produced on this point, but it is recognized that the sero-reaction during infection is not necessarily correlated with the severity of the illness.

Prophylaxis in sewer workers is difficult. In Glasgow, men are warned about the risks of having exposed cuts or scratches; protective clothing is supplied and facilities for washing and disinfection are available. It is unlikely that this will be of much avail, since invasion of the body through the eyes, mouth, and abrasions can be so rapid. Adequate vaccination with an efficient antigen will probably be the ultimate solution. This is highly successful in protecting experimental animals, but is still largely experimental in man.

Summary

In the past three years three sewer workers in Glasgow have died from presumed Weil's disease; one case has been bacteriologically proved.

Evidence of past infection has been found in six out of a total of thirty-six workers.

Virulent leptospirae have been isolated from sewer rats and from sewer slime.

Vaccination is suggested as the only prophylactic measure likely to be efficient.

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TREATMENT OF BRUCELLA MELITENSIS INFECTION WITH PRONTOSIL*

BY

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During the last ten months a number of reports have appeared in English and foreign journals claiming an almost specific effect for prontosil and other sulphonamides in undulant fever. As the treatment of this infection is one of our major therapeutic problems in Malta it was decided to investigate this line more extensively, and under conditions where a rigid scientific control could be maintained.

This note is based on twenty-five cases treated at the Central Hospital, Malta, between August 15 and September 22, 1938. Of these, four were men and twenty-one were women. The ages varied between 14 and 45 years. The majority were seen in the earlier stages, within two or three weeks of the onset of the disease, but in some the infection had been present for a longer period. The series included sixteen cases of the ordinary febrile undulating type; four cases of the "septicaemic" or "malignant" type; and six cases of the mild intermittent type, which is similar to abortus fever as it occurs in England and the U.S.A. The series was fairly representative of undulant fever as it occurs in Malta. The diagnosis was confirmed in every case by an agglutination reaction of over 1 in 100, and in twelve instances by a positive blood culture. As *Brucella abortus* has not been met with in Malta, all the cases may be taken to have been due to the *Br. melitensis*.

The preparation used was prontosil rubrum in eighteen cases, prontosil album in four, and streptocide in three. The average dose was 9 tablets of 0.5 gramme daily for seven days. In five cases treatment had to be stopped on account of intolerance, and in another four it was prolonged for twelve days in an attempt to obtain a decisive result.

Results

In nineteen cases there was no apparent effect on the temperature or on the course of the disease. If the drug was given during the decline of a pyrexial wave the temperature continued to fall *gradually*, to rise again in

* Read at a meeting of the Malta Branch of the British Medical Association, October 24, 1938.